

## **I. Remarks**

Claims 1, 2, 5-8, 33, and 63-70 are pending in the application following entry of this Amendment. Claims 1, 2, 5-8, 33, and 63-64 have been rejected. Claims 65-70 are new. Claims 1, 33, 63, 65, 66, and 70 are the only independent claims pending.

In the interest of furthering prosecution, the claims have been amended without prejudice to pursue additional subject matter in this or any other appropriate patent application.

No new matter has been introduced by the amendments to the claims. Support for the claim amendments is found, for example, as set forth below:

- Support for amending claims 1 and 33 to refer to administration to “the striatum, pallidum, septum, cortex, external capsule, internal capsule, substantia nigra-ventral tegmentum, or at or adjacent to an ependymal or subependymal zone” is found, for example, at page 6, lines 17-22, page 25, lines 26 to 30, page 55, lines 8-14, page 60, lines 2-4, page 71, lines 12-31, page 72, lines 12-19 and page 75, lines 9-18.
- Support for new claim 65 is found, *e.g.*, in claim 1 and at page 51, lines 14-25.
- Support for new claim 66 is found, *e.g.* in claim 1 and at page 41, lines 13-23.
- Support for claim 67 is found in the specification, *e.g.*, at page 26, line 27 to page 27, line 3.
- Support for claim 68 is found in the specification, *e.g.*, at page 60, lines 2-4.
- Support for claim 69 is found, *e.g.*, in the claims as originally filed.
- Support for claim 70 is found, *e.g.*, in claim 1 and in the specification, *e.g.*, at page 22, lines 18-30, at page 55, lines 8-14 and at page 57, lines 23-29.

Each of the Examiner's rejections is addressed below.

### **A. The rejection of Claims 1, 2, 5-8, 33, and 63-64 under 35 U.S.C. § 112**

The examiner has rejected the claims under 35 U.S.C. § 112 for lack of written description for the phrase “functional fragments.” Applicants believe that this rejection is moot in view of the amendment to recite functional fragments “comprising CysX<sub>7</sub>CysX<sub>4</sub>CysX<sub>10</sub>CysXCysX<sub>8</sub>Cys,” which identifies a particular portion of the molecule known to be required for activity. *See* specification at page 28, lines 15-30. Applicants therefore

believe that the current claims are sufficiently described in the specification, and therefore, that this rejection should be withdrawn.

**B. The rejection of Claims 1, 2, 5-8, 33, and 63-64 under 35 U.S.C. § 112**

Applicants believe that the rejection under 35 U.S.C. § 112 is moot as applied to the claims as currently pending.

The examiner had rejected the pending claims on the basis that “the claims encompass an unreasonable number of distinct sites of damage within the CNS, many of which, like the spinal cord, have never demonstrated a nexus to or association with a population of neural progenitor cells.” See 3/28/08 Office Action at page 9. The claims now recite that the TGF- $\alpha$  or functional fragment is administered to the “striatum, pallidum, septum, cortex, external capsule, internal capsule substantia nigra-ventral tegmentum at or adjacent to an ependymal or subependymal zone,” or to the “forebrain or midbrain” of the individual. The forebrain, ependymal or subependymal zones were known to contain multipotent stem cells. See, *e.g.*, page 22, lines 18-30, page 60, lines 2-4. In addition, adult spinal cords were known to contain multipotent cells, as reported, for example, in Weiss *et al.*, “Multipotent CNS Stem Cells Are Present in the Adult Mammalian Spinal Cord and Ventricular Neuroaxis,” *J. Neurosci.* 16(23):7599-7609 (1996). Moreover, Applicants (1) presented examples showing administration to locations including the striatum, septum, cortex, external capsule, and to midbrain structures such as the substantia nigra-ventral tegmentum; (2) demonstrated the presence of proliferating neural cells in the ependymal and subependymal zones following TGF- $\alpha$  administration (see Figures 8A and 8B, 9C and 9D, 10A and 10B, and 11A-11C; (3) reported the presence of migrating cells in the internal capsule (see page 55, lines 8-14) and (4) summarized that administration of TGF- $\alpha$  to the striatum, septum, cortex, and external capsule led to proliferation, migration, maturation and differentiation of newly generated cells into cells exhibiting phenotypic specialization, see page 75, lines 3-19. The rejection for lack of enablement should therefore be withdrawn.

**C. The rejection of pending Claims 1, 2, 5-7, 33, and 63-64 under 35 U.S.C. § 102(a) over Alexi et al., Neuroscience, 78(1):73-86 (1997)**

The examiner has rejected claims 1, 2, 5-7, 33, and 63-65 under 35 U.S.C. § 102(a) over Alexi et al., Neuroscience, 78(1):73-86 (1997). Applicants respectfully submit that Alexi *et al.* is not prior art to the subject application. To qualify as a prior art reference under 35 § 102(a), Alexi *et al.* must have been published “before the invention thereof by the applicant.” 35 U.S.C. § 102(a) (emphasis added). In previous communications, the examiner had cited as a reference under 35 U.S.C. § 102, an abstract co-authored by Applicants, (Reid *et al.*, “Radial migration of subependymal cells in the adult rodent forebrain,” Soc. Neurosci. Abstracts, (1996) Vol. 22(3)). Although the rejection based on Reid *et al.* was previously overcome for the reasons discussed in the Amendment Under 37 C.F.R. § 1.111 dated November 26, 2002, at pages 4-5, the Reid *et al.* abstract establishes that Alexi *et al.* was not published prior to Applicants’ invention. The Reid *et al.* abstract evidences that Applicants conceived and reduced to practice any elements of the instant invention disclosed by Alexi *et al.* Thus, Applicants respectfully submit that the rejection based on Alexi *et al.*, Neuroscience 78(1) should be withdrawn.

## **II. Co-Pending Applications**

Applicants would like to bring to the attention of the examiner co-pending applications 10/167,384 and 09/ 129,028, and prosecution thereof.

## **III. Summary**

In view of the Amendment of the Claims and the Remarks in support of patentability, allowance of the pending claims is respectfully requested. The Examiner is invited to telephone the undersigned at (619) 744-2264 for any reason to advance the prosecution of the application.

Respectfully submitted,

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